INTERSEX

BY

ATTIA ABDALLA ATTIA

PROF. & HEAD OF

DERMATOLOGY & ANDROLOGY

DEPARTMENT

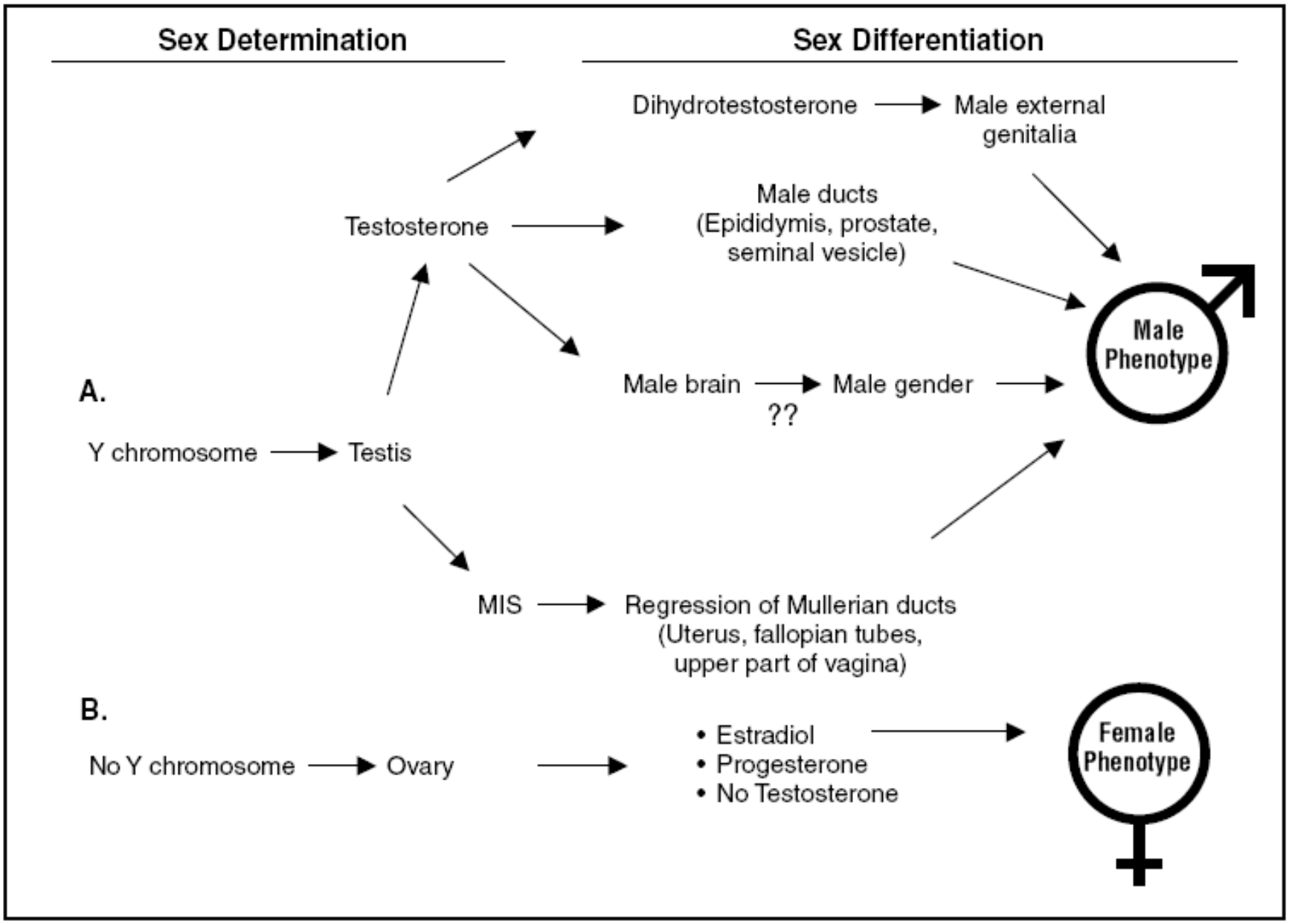
AL- AZHAR FACULTY OF MEDICINE

INTRODUCTION

- **Genetic sex**: (**XY or XX**)
- **Gonadal sex : (internal genitalia)**
- **Phenotypic sex : (external genitalia).**
- **Gender sex : (brain sex)**
- **Rearing sex : (denotes cultural characteristics)**
- **Legal sex: (consists only of male and female, despite the infinite spectrum of gender and sexual variations.)**

N.B.

Genetic sex occurs at time of fertilization→ Gonadal sex.


Sex Determination
Sex Differentiation
Dihydrotestosterone
Male external genitalia
Testosterone
Male ducts (Epididymis, prostate, seminal vesicle)
Male Phenotype
A.
Male brain
Male gender
??
Y chromosome
Testis
MIS
Regression of Mullerian ducts (Uterus, fallopian tubes, upper part of vagina)
B.
No Y chromosome
Ovary
• Estradiol
• Progesterone
• No Testosterone
Female Phenotype

- Brain exposure to androgens during critical periods of development results in masculinization of behaviors that typically show sex differences.

- **Lahr et al., (1995)** reported that sex-determining genes themselves (such as SRY) are expressed in specific regions of the brain
- This evidence suggests that genetic influences play a role in the development of brain sexual orientation.

Intersex syndrome

- It is an intermingling of characteristics of both sexes which may be:

  @ Anatomical (DSD)

  @Psychological(Gender Identity Disorders)

  @ Combinations

- It results from some defect in the embryonic development.

INTERSEX

- IN (2006)

The **Intersex Society of North America**

eliminated the term "intersex" ,

and replaced it with

“Disorders of Sex Dvelopment"

(DSD)

in order to avoid conflicting anatomy with gender identity (transexualism)

THE DIFFRENCE

DSD

- It is a group of conditions where there is a discrepancy between the external genitals and the internal genitals .

TRANSSEXUALISM

- A gender identity disorder is one in which a person wants to be the opposite sex. The person believes that he or she is **"trapped"** in a body of the wrong sex.

THE GENDER IDENTITY DISORDER:

- Based on the person's sensations

  (what you think you are ?)

  - a man trapped in a woman body or
  - a woman trapped in a man body,

- This is established by the age of 3ys.
- There is no prevention for gender identity disorder.

Causes of the Gender identity disorder:

- Unknown,
- Some theories suggest the causes:

  1- Chromosomal abnormality

  2- Hormonal imbalance

  3- Early parent-child bonding problems

  4- Harmful child-rearing practices

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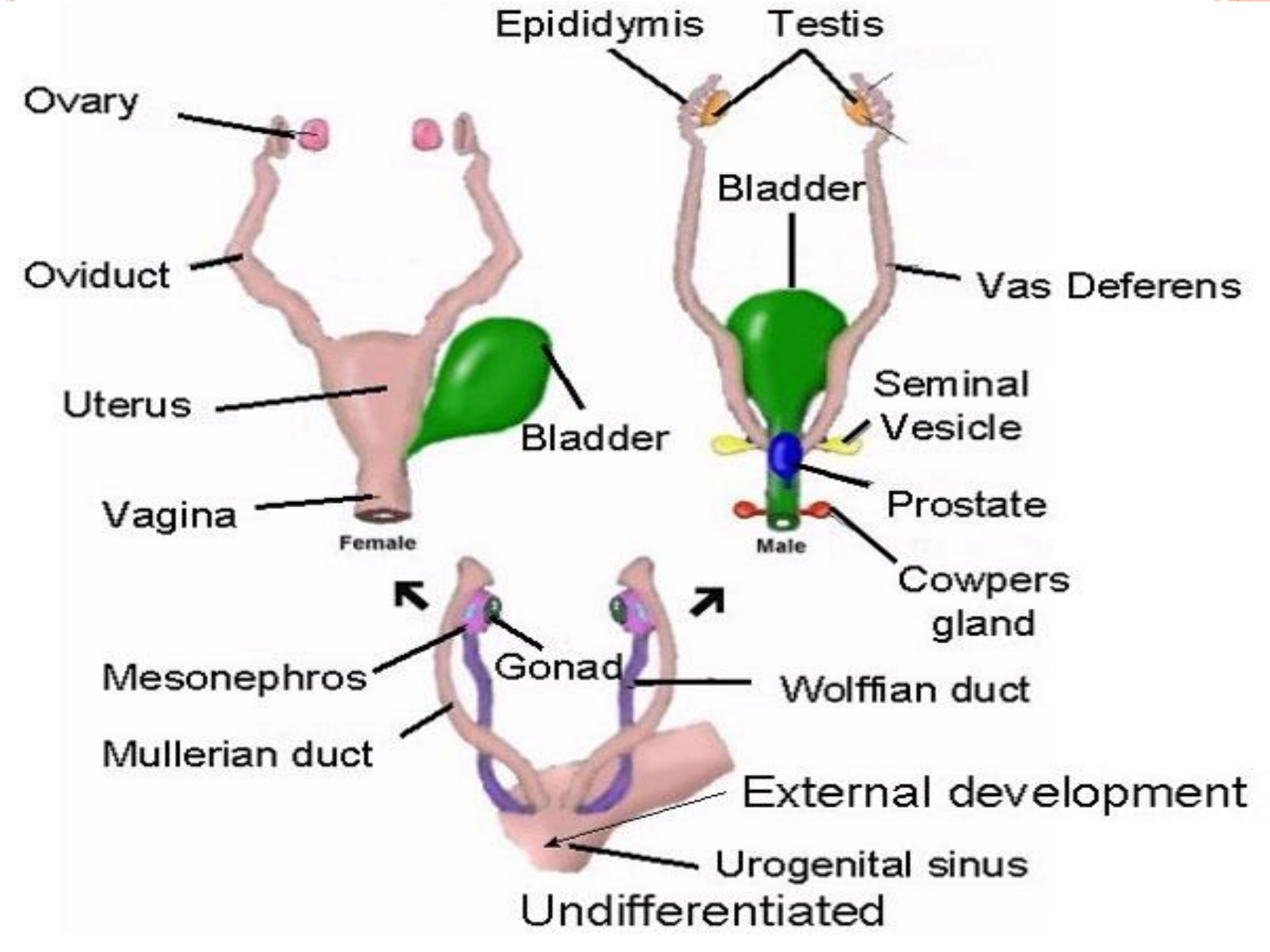
EMBRYOLOGY

- Gonadal ridge (*SRY*) →Internal genitalia (Gonads) (testes).
- Wollfian duct (***testosterone***)→ Internal ducts (Epid,Vas,SV.).
- MULLERIAN d.*(MIS)* ----Disappear in male MD in female ---- uterus &upper tow thirds of the vagina
- Both **male** and **female** fetuses usually have at least one **X** chromosome gene this gives them the capacity to *recognize* and *react to* androgens.


Epididymis
Testis
Ovary
Bladder
Oviduct
Vas Deferens
Uterus
Seminal
Vesicle
Bladder
Vagina
Prostate
Female
Male
Cowpers
gland
Mesonephros
Gonad
Wolffian duct
Mullerian duct
External development
Urogenital sinus
Undifferentiated

DSD

- **DSD is a group of conditions where there is a discrepancy between the external genitals and the internal genitals (the testes and ovaries).**
- **It results from some defect in the embryonic development**
- **Up to 8weeks of gestation the gonad is indifferent (bipotential)**

DSD

DSD is present in about 1% of the population.

Classification:

- **1. True hermaphroditism .**
- **2. Pseudo- hermaphroditism:**
  - **a. Male pseudohermaphroditism.**
  - **b. Female pseudohermaphroditism**
- **3. Pure gonadal agenesis**
- **4. Gonadal dysgenesis:**
  - **a) Klinefelter's syndrome.**
  - **b) Noonan's & Turner's syndromes.**

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TRUE HERMAPHRODITISM

- The person have both ovarian and testicular tissue OR (an ovotestis), OR one ovary and one testis.
- The person may have XX chromosomes, XY chromosomes, or both.
- The external genitals may be ambiguous or may appear to be female

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- :

♂Male pseudohermaphrodite

- **Genetic sex: XY**
- **Gonadal sex: Testes.**
- **Phenotypic sex:**

  external genitals are :

  -incompletely formed,

  -ambiguous, or

  -clearly female.

Male Pseudo-hermaphroditism due to:

A) AIS (ANDROGEN INSENSETIVE SYNDROME)

B)↓ Androgen due to:

1- ↓ Androgen production.

2- ↓ 5 alpha reductase SO ↓ DHT.

C) Isolated deficiency of MIS

- **It is a rare syndrome and usually does not present in the newborn period because the genitalia appear to be those of a male with undescended testes.**

C)

A) ANDROGEN INSENSETIVE SYNDROME

(DEFECTIVE ANDROGEN RECEPTORS)

- In **AIS** :

- functioning Y ⟹ no female internal organs,

- abnormal **X** ⟹ the body unable to respond to androgens completely or partially

- *** CAIS,** the external genital of the female .

- *** PAIS,** the ext. genital ranged from male to female.

SYNONYMS

- Androgen Insensitivity Syndrome,
- Testicular Feminization Syndrome ,
- **Defective Androgen receptors**
- Androgen Resistance Syndrome,


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Grading of AIS

Grade 1	PAIS	Male genitals, infertility
Grade 2	PAIS	Male genitals but mildly 'under-masculinized', isolated hypospadias
Grade 3	PAIS	Male genitals but more severely 'under-masculinized' (perineal hypospadias, small penis, cryptorchidism i.e. undescended testes, and/or bifid scrotum)
Grade 4	PAIS	**Ambiguous genitals,** severely 'under-masculinized' at puberty the breast well formed(phallic is between a penis and a clitoris)
Grade 5	PAIS	**Female genitals** (including separate urethral and vaginal orifices, enlarged clitoris)
Drade 6	PAIS	**Female genitals** with pubic/underarm hair
Grade 7	**C**AIS	**Female genitals** with little or no pubic/underarm hair

Hypogonadotrophic Hypogonadism

Grade 1

PAIS

Grade 4

PAIS


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MANAGEMENT

Male Pseudo-hermaphroditism

AIS (ANDROGEN INSENSETIVE SYNDROME)

-Remove testes early because morbidity is minimal in a young child.
-Hormonal replacement at age of puberty .
-Vaginoplasty later may be required,
-Many of the girls have an adequate vagina

Causes of Male Pseudohermaphroditism

A)AIS

B) ↓ Androgen due to:

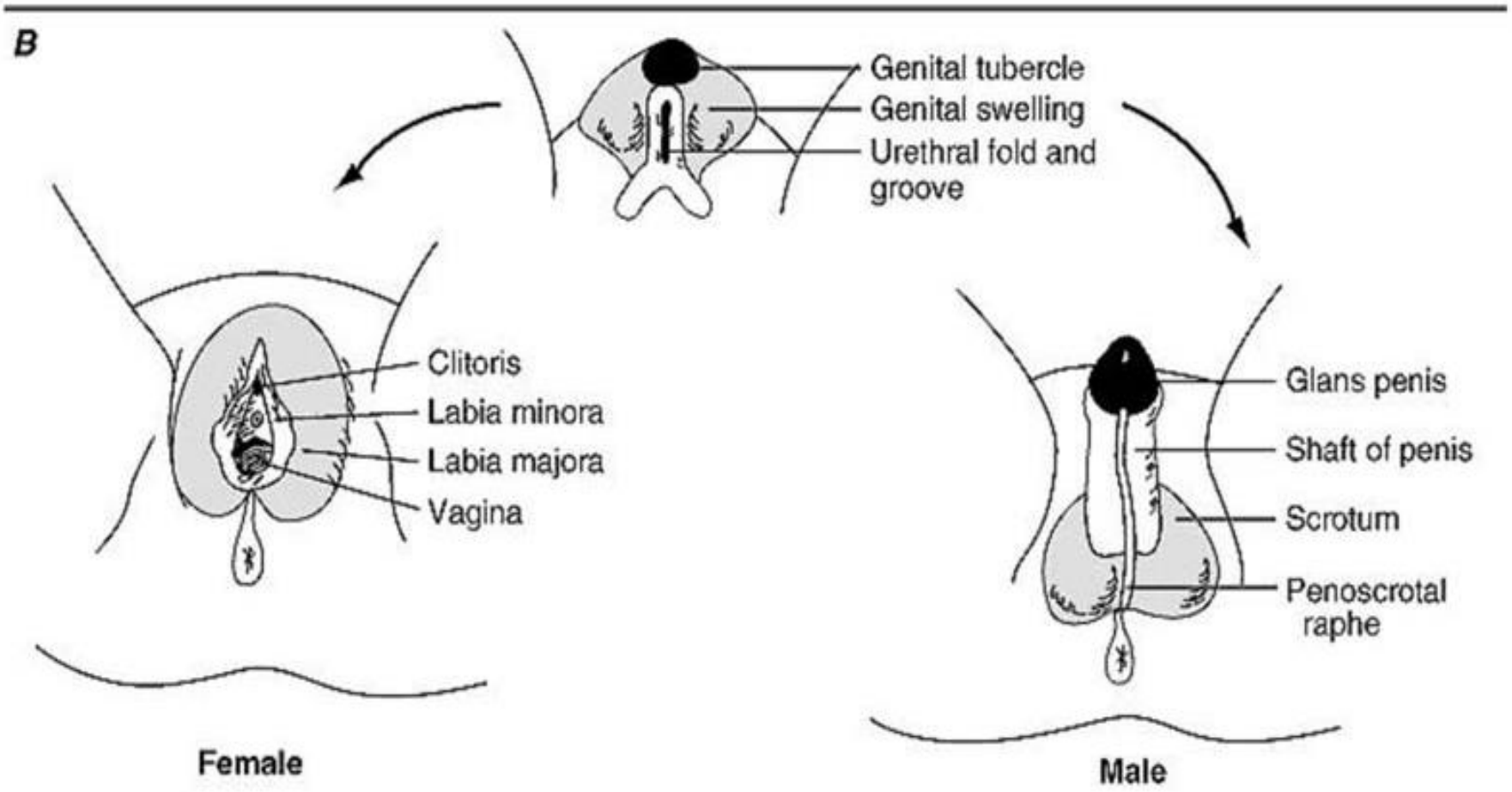
1- ↓ Androgen production.

2- ↓ 5 alpha reductase SO ↓ DHT.

C) Isolated deficiency of MIS

1- ↓Androgen synthesis

- **A group of enzyme deficiencies → inborn errors of testosterone biosynthesis.**
- **Inherited AR or X-linked recessive.**
- **Atypical congenital adrenal hyperplasia can fall in this category.**



- **Genital Tubercle (*DHT*) → Penis**
- **Genital Swelling (*DHT*) → fuse to form Scrotum**

2-↓ 5 ALPHA REDUCTASE ENZYME → DHT

1- Normal wollfian duct structures (Epid.,Vas, SV.) testosterone

2- Abnormalities in external genitalia & prostate (DHT).

3- This will lead to :

Pseudovaginal Perineoscrotal Hypospadius.

EARLY :BEFOR PUBERTY

- Prineoscrotal hypospadius
- Vaginal pouch open in the urethra.
- Bifid scrotum
- Serum testosterone & LH are normal.

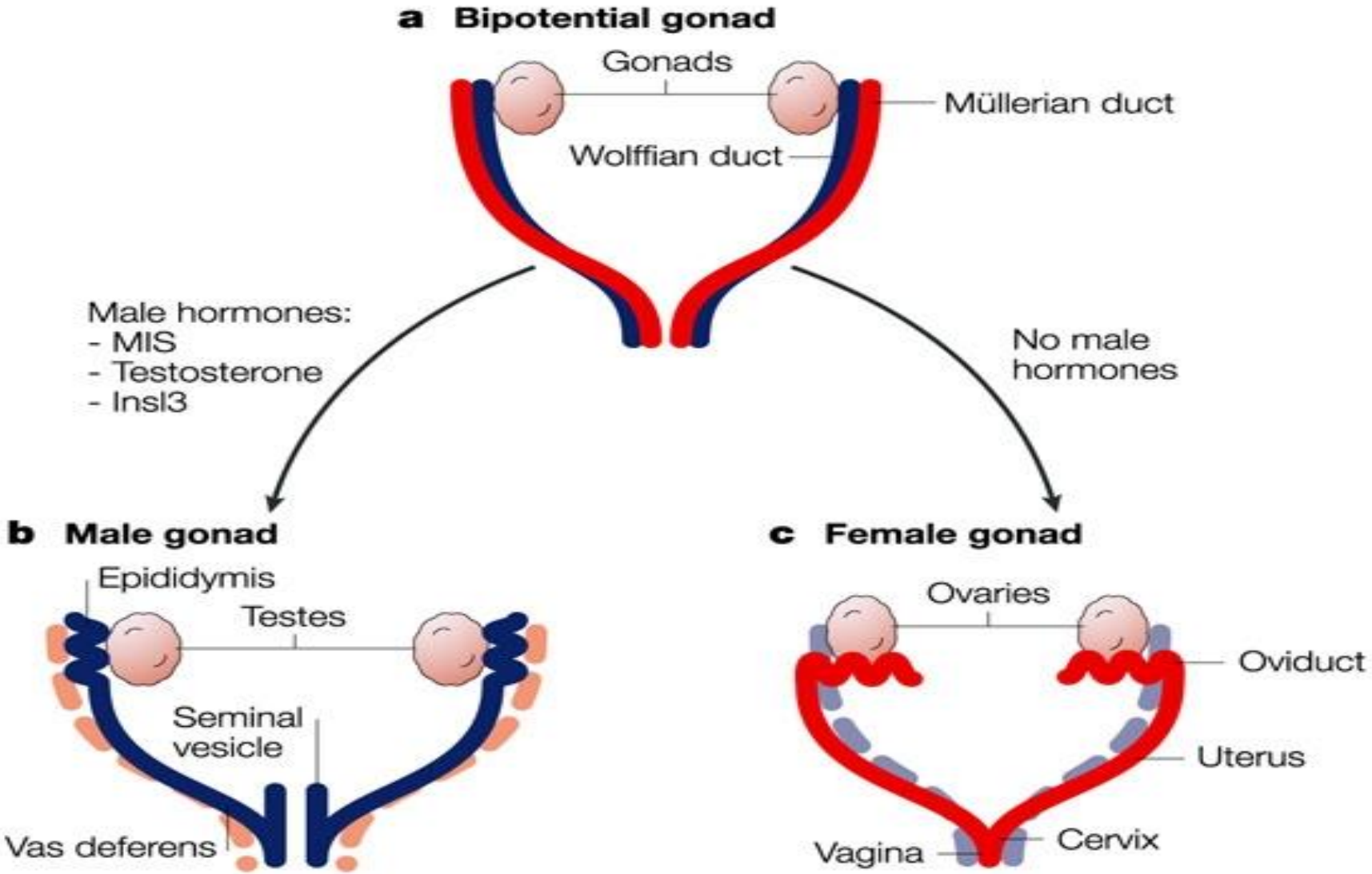
At puberty:

- Virilization occurs & become male.
- Testes in labial fold or inguinal.
- Normal spermatogenesis (norm. testo.)

MANAGEMENT

OF PSEUDOVAGINAL PERINEOSCROTAL HYPOSPADIUS DUE TO↓ 5 ALPHA REDUCTASE ENZYME

- An early gonadectomy and feminizing genitoplasty are recommended in infancy.



Nature Reviews | Genetics

C) Isolated deficiency of MIS

It is a rare syndrome presented as a phenotypic male with an inguinal hernia on one side and an impalpable gonad in other side. Herniorrhaphy reveals a uterus and fallopian tube in the hernia sac

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♀FEMALE PSEUDOHERMAPHRODITE

- **Genetic sex: XX**
- **Gonadal sex: ovaries**
- **Phenotypic sex: external genitals appear male :**

-The labia fuse,
-The clitoris enlarges (like a penis).

CAH

♀FEMAL PSEUDOHERMAPHRODITE

- **Intrauterine exposure** of female fetus to **ANDROGEN** due to :

  @CAH (60% of all intersex cases.)

  @ Maternal tumour.

  @ Androgen containing medication .

CONGENITAL ADRENAL HYPERPLASIA

- **CAH** A group of inherited disorders of the adrenal gland.

Causes:

- ↓ 21-hydroxylase enzyme for cortisol and aldosterone formation →↑ACTH→ ↑androgen → virilization.
- It can affect both:

  Girls → female pseudohermaphrodite

  Boys → (precocious puberty).

NB:Salt-wasting nephropathy occurs in 75% of infants born with CAH

Female pseudohermaphrodite (CAH)

- Internal organs normal:

(ovaries, uterus, and fallopian tubes)

-External changes:

- Ambiguous genitalia (male > female)
- Deep voice
- Early appearance of pubic and armpit hair
- Excessive hair growth body and face .

Treatment of CAH

- **The goal of treatment is to return hormone levels to normal.**

This is done by:

Daily administration (dexamethasone, or hydrocortisone).

- **Severe cases:**

- Early: clitroplasty

- Late: vaginoplasty.

MANAGEMENT OF DSD

Management of a child with DSD is critical and should involve team with careful consideration of :

- proper diagnosis,
- hormonal treatments,
- potential surgical interventions, and
- psychosocial monitoring, with the goal of optimal psychosexual development.

Causes of Pseudo-hermaphroditism

1-MALE

A) AIS (ANDROGEN INSENSETIVE SYNDROME)

B)↓ Androgen due to:

1- ↓ Androgen production.

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C) Isolated deficiency of MIS

2- FEMAL

Intrauterine exposure of female fetus to **ANDROGEN**

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3. PURE GONADAL AGENESIS

BILATERAL CONGENITAL ANORCHIA


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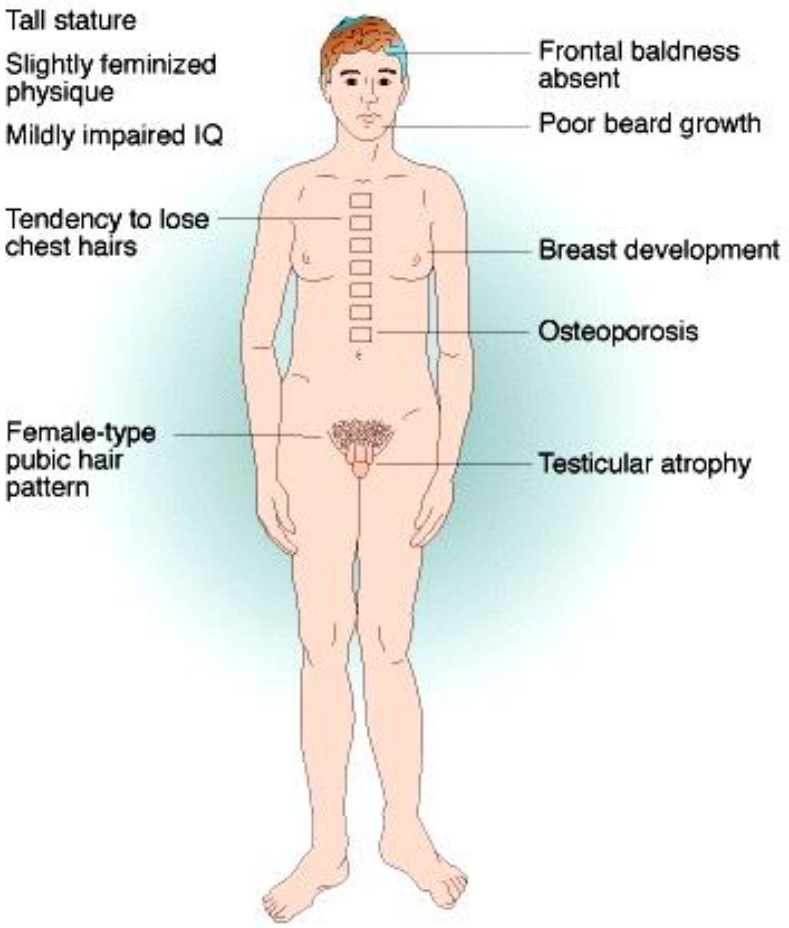
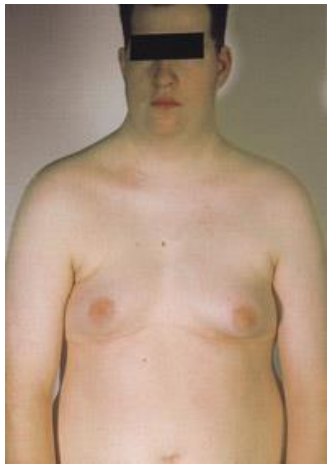
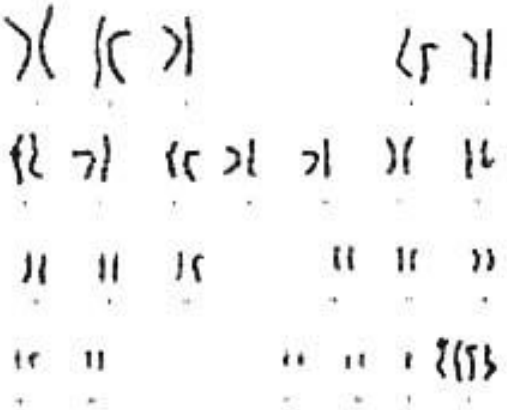
4. Gonadal dysgenesis:

Klinefelter's syndrome







2. Gonadal dysgenesis:

Noonan's syndrome

- **Male phenotypic equivalent of Turner's(45 x0)**
- **Cryptorchidism in 77 % of cases.**
- **Manifestation:**

  - short stature

  - webbed neck

  - low set ears

  - hypertension

  - cubitus vulgus

  - pulmonary stenosis

Thank you

PRECOCIOUS PUBERTY OF BOYS (CAH)

- Boys won't have any obvious problems at birth.
- Enter puberty as early as 2-3 years of age ((precocious puberty).

Changes may include:

- Deep voice
- Early appearance of pubic and armpit hair
- Early development of masculine characteristics
- Enlarged penis
- Small testes
- Well-developed muscles